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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/501,730	02/10/2000	Merry R. Sherman	MVIEW.0050A	4303

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EXAMINER	
PAK, YONG D	
ART UNIT	**PAPER NUMBER**
1652	29

DATE MAILED: 12/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/501,730	SHERMAN ET AL.	
	Examiner	Art Unit	
	Yong Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-28 and 33-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,17-25,27,28 and 33-36* is/are rejected.

7)☒ Claim(s) *8 and 26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *20 & 23* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 20, 2002 has been entered. The amendment filed on September 20, 2002, canceling claims 10 and 29-32, adding claims 34-37 and amending claims 5, 9, 12, 14, 16, 17, 19 and 33, has been entered.

Claims 1-9, 11-28 and 33-37 are pending.

Election/Restrictions

Claims 11-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 6.

Response to Amendment

The declaration under 37 CFR 1.132 filed September 20, 2002 is sufficient to overcome the rejection of claims 1-8, 17-28 and 33 based upon Puricase™ Registration No. 2,246,623.

Information Disclosure Statement

The information disclosure statement filed November 12, 2002 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language, DD 279 486 A1 and JP 09154581. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 6 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Aleman et al.

Aleman et al. (U.S. Patent 5,811,096) teach that Poloxamer 188 and Polysorbate 80 aids in reducing the degree of aggregation of urate oxidase in solution by as much as three fold, resulting in a stable pharmaceutical composition (Figure 1, Composition 2 and Column 1, lines 5-10). It can be construed that Aleman et al teach an uricase substantially free of aggregates larger than octamers (figures1-2, Column 5, lines 1-9 and claims 1-23). Regarding claims 4 and 6, Aleman et al. teach that the protein can be obtained from a strain mutated by genetic engineering and produced from a cell

(Column 2, lines 53-57). Therefore, the teachings of Meredith anticipate claims 1, 4, 6 and 33.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 and 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aleman et al. in view of Wu et al.

Aleman et al. Teach a uricase substantially free of large aggregates, as discussed above.

The difference between the reference of Aleman et al. and the instant invention is that the reference of Aleman et al. does not teach a porcine urate oxidase.

Wu et al. (form PTO-1449) teach recombinant porcine urate oxidase from *S. scrofra* (page 9412). Wu et al. also teach recombinant *P. hamadryas* urate oxidase (page 9412-9413). Regarding claim 33, patentability of a product does not depend on the method used in producing the product (MPEP 2113).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make the composition of Aleman et al. using the uricase of Wu et al. The motivation is to stabilize a composition comprising a mammalian uricase for use as a therapeutic in man. One of ordinary skill in the art would have had a reasonable expectation of success since Aleman et al. successfully stabilized a composition comprising an uricase.

Claims 1-7, 9 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aleman et al. in view of Wu et al.

Aleman et al. teach a uricase substantially free of large aggregates, as discussed above.

The difference between the reference of Aleman et al. and the instant invention is that the reference of Aleman et al. does not teach an uricase wherein tyrosine 97 has been replaced by a histidine.

Wu et al. teach that baboon, porcine and mouse uricases are highly conserved (page 9413, 2nd column and Fig 2 –b). Mouse and porcine uricase has a His at position 97, while baboon has a Tyr at position 97. A portion can be construed as one or more amino acids.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a chimeric uricase by replacing Tyr 97 of the baboon uricase with Try97 of the porcine uricase and stabilize the protein by the method taught by Aleman et al.. One would be motivated to replace a residue with a conserved residue because conserved amino acids very often impart the characteristic property of an enzyme. One of ordinary skill in the art would have had a reasonable expectation of success since site specific mutations are routinely performed in the art.

Claims 1 and 17-25 and 27-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aleman et al. in view of Delgado et al.

Aleman et al. teach uricase substantially free of large aggregates, as discussed above. Further, Aleman et al. teach a composition comprising uricase stabilized by lyophilization (Columns 4-5).

The difference between the reference of Aleman et al. and the instant invention is that the reference of Aleman et al. does not teach an uricase conjugated to poly(ethylene glycol) and monomethoxy-PEG (Column 2).

Delgado et al. (U.S. Patent 5,880,225 – form PTO 1449) teach uricase conjugated to PEG (abstract and claim 1). Delgado et al. Also teach a uricase conjugated to monomethoxy-PEG (claim 2). Delgado et al. Teach that a NH2 of a lysine group can be used to link the PEG (Column 1, lines 25-26). Delgado et al. Teach that PEG can range from .2 kDa to 20 kDa (Column 1, lines 15-25). Delgado et al. Teach that different molar ration of PEG to protein can be used (Column 3, lines 15-35). Delgado et al. Teach the PEG is linear (Column 1, lines 16-17). Delgado et al. Teach that PEG modification extends plasma half lives, increases the bio-availability of enzymes and reduces antigenicity of proteins (Column 1, lines 34-50).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make the composition of Aleman et al. using the conjugate of Delgado et al. The motivation is to further stabilize a composition comprising the protein for use as a therapeutic in man. One of ordinary skill in the art would have had a reasonable expectation of success since Aleman et al. and Delgano et al. successfully stabilized a composition comprising an uricase.

Claims 1 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al. in view of Ansaldi et al.

The examiner notes that the reference of Ansaldi et al. (U.S. Patent Application Publication US 2002/0010315) qualifies as prior art under the Intellectual Property and High Technology Technical Amendment Act of 2002.

Wu et al. teach that porcine urate oxidase is six amino acid residues shorter than that of rat uricase (page 9414, 2nd column) but the two uricases are highly conserved throughout the coding region (page 9413, 4th paragraph).

The difference between the reference of Wu et al. and the instant invention is that the reference of Wu et al. does not teach an uricase free of large aggregates.

Ansaldi et al. teach a method of separating mammalian enzyme monomers from a mixture containing multimers (abstract, [0009] – [0010], [0020], and [0026] - [0033]. Ansaldi et al. teach that purification of recombinant proteins free of inactive, misfolded, insoluble, and or soluble dimers, multimers and disulfide-linked aggregates is Figures 1-6 teach that the isolated protein monomer is substantially free of aggregates or multimers, comprising less than 2% of multimers.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a functional uricase of a smaller size by deleting residues from both N –terminus and to remove large aggregates as taught by Ansaldi et al. The motivation is to determine whether residues at the N-terminus are important for uricase activity and to use a smaller functional fragment of uricase in view of convenience and to isolate uricase substantially free of large aggregates to decrease immunogenicity or increase bioreactivity. One of ordinary skill in the art would have had a reasonable expectation of success since site specific mutations are routinely performed in the art.

Claims 1, 17, 35, 27 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aleman et al. in view of Delgado et al. in further view of Ansaldi et al.

The reference of Aleman et al. in view of Dalgado et al. teach a pharmaceutical composition PEG-uricase.

The difference between the two reference and the instant invention is that the two references in combination do not teach a composition wherein said composition contains no more than about 2% aggregates larger than octamers.

Ansaldi et al. (U.S. Patent Application Publication US 2002/0010315) teach a method of separating mammalian enzyme monomers from a mixture containing multimers, as discussed above.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to the method of Ansaldi et al. to further purify uricase wherein said protein contains less than 2% of large aggregates. The motivation is to isolate uricase substantially free of large aggregates to decrease immunogenicity or increase bioreactivity. One of ordinary skill in the art would have had a reasonable expectation of success since Ansaldi et al. successfully removed large aggregates from a composition comprising a mixture of multimers.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 703-308-9363. The examiner can normally be reached on 8:00 A.M. to 4:30 P.M weekdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Yong Pak
Patent Examiner

December 2, 2002

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